BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

COMBINED DECLARATION AND POWER OF ATTORNEY (Original, Design, National Stage of PCT or CIP Application)	ATTORNEY'S DOCKET NO. 30307

As a below named inventor I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name, I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

SINGLE COPY GENOMIC HYBRIDIZATION PROBES AND METHOD OF GENERATING SAME

the specification of which: (complete (a), (b) or (c) for type of application)

REGULAR OR DESIGN APPLICATION

(a) [ ] is attached hereto.
(b) [X] was filed on May 16, 2000 as Application Serial No. 09/573,080 and was amended on _____ ____ (if applicable).

PCT FILED APPLICATION ENTERING NATIONAL PHASE

(c) ☐ was described and claimed in International Application No. _____ filed _____ and as amended on _____ (if any).

ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56(a).

[ ] In compliance with this duty there is attached an information disclosure statement. 37 CFR 1.97.

PRIORITY CLAIM

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:
(complete (d) or (e))

(d) [X] no such applications have been filed.
(e) [ ] such applications have been filed as follows

EARLIEST FOREIGN APPLICATION(S), IF ANY FILED WITHIN 12 MONTHS PRIOR TO SAID APPLICATION

Country	Application No.	Date of Filing	Date of Issue	Priority Claimed
				☐ YES ☐ NO
				☐ YES ☐ NO
				☐ YES ☐ NO

ALL FOREIGN APPLICATION(S), IF ANY FILED MORE THAN 12 MONTHS PRIOR TO SAID APPLICATION

PROVISIONAL

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States application(s) listed below:

Application Serial No.	Filing Date	Status (patented, pending, abandoned)

CONTINUATION-IN-PART

(Complete This Part Only If This Is A Continuation-In-Part Application)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56(a), which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application:

Application Serial No.	Filing Date	Status (patented, pending, abandoned)

POWER OF ATTORNEY

As a named inventor, I hereby appoint the following attorney(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

Robert D. Hovey	19,223	Thomas B. Luebbering	37,874
Warren N. Williams	19,156	Andrew G. Colombo	40,565
Stephen D. Timmons	26,513	Scott R. Brown	40,535
John M. Collins	26,262	Tracy L. Bornman	42,347
Thomas H. Van Hoozer	32,761	Tracey S. Truitt	43,205

SEND CORRESPONDENCE TO:	DIRECT TELEPHONE CALLS TO:
HOVEY, WILLIAMS, TIMMONS & COLLINS 2405 Grand, Suite 400 Kansas City, Missouri 64108	(816) 474-9050

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor	JOAN H. M. KNOLL	
Inventor's Signature	Joan H. M. Knoll, Ph. D.	
Date 8.29.00	Country of Citizenship	~~USA~~ CANADA JHMK 8/29/00
Residence	12226 Gillette Road, Overland Park, KS 66213	
Post Office Address	12226 Gillette Road, Overland Park, KS 66213	
Full name of second joint inventor, if any	PETER K. ROGAN	
Inventor's Signature	Peter K. Rogan PhD	
Date 8/29/00	Country of Citizenship	USA
Residence	12226 Gillette Road, Overland Park, KS 66213	
Post Office Address	12226 Gillette Road, Overland Park, KS 66213	

Applicant or Patentee: JOAN H. M. KNOLL and PETER K. ROGAN	Attorney's Docket No.: 30307
Serial or Patent No.: 09/573,080	
Filed or issued: May 16, 2000	
For: SINGLE COPY GENOMIC HYBRIDIZATION PROBES AND METHOD OF GENERATING SAME	

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) AND 1.27(d)) - NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION: CHILDREN'S MERCY HOSPITAL

ADDRESS OF ORGANIZATION: 2401 Gillham Road, Kansas City, MO 64108

TYPE OF ORGANIZATION:

[ ] University or other institution of Higher Education
[X] Tax Exempt Under Internal Revenue Service Code (26 USC 501(a) and 501(c)(3)
[ ] Nonprofit Scientific or Educational Under the Statute of State of the United States of America; Name of State _____, Citation of Statute _____
[ ] Would qualify as Tax Exempt Under Internal Revenue Service Code (26 USC 501(a) and 501(c)(3) if located in the United States of America
[ ] Would qualify as Nonprofit Scientific or Educational under Statute of the United States of America if located in the United States of America; Name of State _____, Citation of Statute _____

I hereby declare that the above-identified nonprofit organization qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees under Section 41(a) and (b) of Title 35, United States Code with regard to the invention entitled SINGLE COPY GENOMIC HYBRIDIZATION PROBES AND METHOD OF GENERATING SAME by Inventor(s) JOAN H. M. KNOLL, PETER K. ROGAN, described in application serial no. 09/573,080, filed May 16, 2000.

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above-identified invention. If the rights held by the nonprofit organization are not exclusive, each individual, concern or organization having rights to the invention is listed below*, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).
***NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)**

FULL NAME N/A
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing therefrom, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: Randall L. O'Donnell, Ph.D.	
TITLE OF PERSON OTHER THAN OWNER President and CEO	
ADDRESS OF PERSON SIGNING 2401 Gillham Road, Kansas City, MO 64108	
SIGNATURE Randall O'Donnell	DATE 8/9/00

ASG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Docket No. 30307CNT1
KNOLL, JOAN et al.	
Serial No. :	Group Art Unit No.
Filed:	
SINGLE COPY GENOMIC HYBRIDIZATION PROBES AND METHOD OF GENERATING THE SAME	Examiner:

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

DECLARATION

I, PETER K ROGAN declare and state as follows:

1. I am one of the inventors of the subject matter described and claimed in the above-identified patent application. A copy of my curriculum vitae is attached hereto as Exhibit A.

2. This declaration is being submitted by us pursuant to 37 C.F.R. § 1.132 in order to submit evidence pertaining to what is described in the application and its significance to those of ordinary skill in the art.

3. The claims are directed to a nucleic acid hybridization probe which will hybridize to a nonrepetitive portion of target nucleic acid, said probe comprising a labeled, single copy human nucleic acid sequence of known sequence, said probe having a length of at least about 2000 nucleotides, said probe being free of the repeat sequences identified as SEQ ID Nos. 1-428 and 447-479 and subsequences thereof, said subsequences containing at least 17 nucleotides, at

least a portion of the human nucleic acid sequence being derived either from an intron or an intergenic region wherein an intergenic region begins either upstream of the transcription initiation site or downstream of the polyadenylation site, and said probe being complementary to a non-repetitive portion of the target.

4. In the most recent Office Action for the application upon which this continuation application is based, the present claims were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, it was alleged that the probes disclosed in the application did not constitute a representative number of species to meet the written description requirement.

5. The claims at issue are not limited to any specific sequence but rather, the claims are directed to genus of probes that include any nucleic acid hybridization probe which will hybridize to a nonrepetitive portion of target nucleic acid. However, the probes are limited in several ways: each probe must comprise a labeled, single copy human nucleic acid sequence of known sequence; each probe must have a length of at least about 2000 nucleotides; each probe must be free of the repeat sequences identified in the application as SEQ ID Nos. 1-428 and 447-479 and 17 nucleotide subsequences therof; at least a portion of the human nucleic acid sequence must be derived either from an intron or an intergenic region wherein an intergenic region begins either upstream of the transcription initiation site or downstream of the polyadenylation site; and, each probe must be complementary to a non-repetitive portion of the target.

6. The application contained an enabling description as to how one of skill in the art would make single copy probes in accordance with the claims. At least 9 probes are sufficiently disclosed to be considered in the question of whether a representative number of species have been sufficiently described. In this respect, the Examiner noted that a total of 8 probes were sufficiently described. However, this total included only 2 of the 3 NECDIN probes provided as examples in the application. Accordingly, the sequence listing of probes contained herein includes 9 rather than 8 probes.

7. In fact, I personally generated the 9 probes resulting from the primer pairs of SEQ ID NOS. 429-446. To do so, I used the used no more than the specification of the present application and the knowledge available to those of skill in the art at the time the application was filed. Some particularly relevant references include Schuler, GD, *Electronic PCR: Bridging the Gap Between Genome Mapping and Genome Sequencing*; 16(11) Trends Biotechnol.; 456-459 (Nov. 1998); Cooper, DN, *Mapping the Human Genome*; 37(3) Ann. Genet.; 101-106 (1994); J. Riley, et al., *A Novel, Rapid Method for the Isolation of Terminal Sequences From Yeast Artificial Chromosome (YAC) Clones*; 18(10) Nucleic Acids Res., 2887-2890, (May 25, 1990); and JF Gusella, et al., *Sequence-Tagged Sites (STSs) Spanning 4p16.3 and the Huntington Disease Candidate Region*; 13(1) Genomics, 75-80, (May 1992). These 9 sequences are provided herein in Patent In format and are designated as SEQ ID NOS. 480-488.

8. I have been informed that the Office Action did not contain a rejection based on the enablement of the claims. It is my understanding that this means that the specification teaches one of ordinary skill in the art how to make and use the claimed invention.

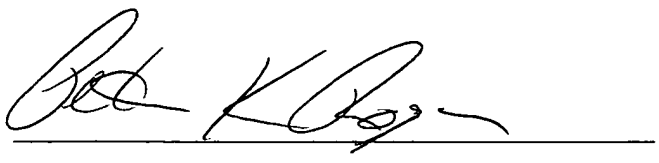
9. One of ordinary skill in the art would be able to make and use of the entire claimed genus of probes using no more than ordinary skill in the art available at the time the application was originally filed by following the enabling disclosure of the specification of the application.

10. This would be done by comparing the sequence of a known target sequence with known repeat sequences from the corresponding genome. In this case, the repeat sequences have already been identified as SEQ ID NOS 1-427 and 447-479 as well as 17mer fragments thereof. Once the repeat sequences of the target sequence have been identified, all that is left is to define the regions between adjacent repeat sequences. This provides the sequences of the probes which are literally, the sequences between adjacent repeat sequences. The target sequence can come from any sequence in the genome.

11. To determine if the identified sequence between adjacent repeat sequences was covered by the claims, one would merely see if the remaining limitations of the claim were all met.

12. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and further that those statements were made with the knowledge that willful, false statements and the like are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and such willful false statements may jeopardize the validity of any patents issued from the patent application.

Date: 1/20/2004



PETER ROGAN

9.20.00

RECORDATION FORM COVER SHEET
PATENTS ONLY

The Assistant Commissioner of Patents
Washington, D.C. 20231
Attention: Assignment Branch

Please record the attached original document or copy thereof.

09-26-2000
101471618

1. Name of Conveying Party(ies):

JOAN H. M. KNOLL
PETER K. ROGAN

2. Name and address of Receiving Party(ies):

CHILDREN'S MERCY HOSPITAL
2401 Gillham Road, Kansas City, MO 64108

3. Nature of Conveyance:

[X] Assignment [ ] Security Agreement [ ]Merger
[ ] License [ ] Change of Name [}Other

Execution Date of Document: August 29, 2000

4. If this document is being filed together with a new application, the execution date of the application is ___

A. Patent Application Numbers: 09/573,080

B. Patent Numbers:

5. Mail correspondence concerning the document to:

John M. Collins
HOVEY, WILLIAMS, TIMMONS & COLLINS
2405 Grand Boulevard
Suite 400
Kansas City, MO 64108-2519

6. Total Number of Applications and Patents Involved: 1.

7. A check for the total fee (37 CFR 3.41) is enclosed: $40.00.

8. The Commissioner is hereby authorized to charge any additional fees required for recordation of the enclosed document. or credit any overpayment, to Deposit Account No. 19-0522.

9. To the best of my knowledge and belief, the foregoing information is true and correct, and any attached copy is a true copy of the original document.

Respectfully submitted,

09/21/2000 WKOROMA 00000040 09573080
01 FC:581 40.00 OP

John M. Collins, Reg. No. 26,262

Date September 14, 2000

Total number of pages, including cover sheet and document 4

(Docket No. 30307)

ASSIGNMENT

WHEREAS, WE, JOAN H. M. KNOLL of 12226 Gillette Road, Overland Park, KS 66213 and PETER K. ROGAN of 12226 Gillette Road, Overland Park, KS 66213, have jointly invented certain new and useful improvements in

SINGLE COPY GENOMIC HYBRIDIZATION PROBES

AND METHOD OF GENERATING SAME

for which we are about to make application for Letters Patent of the United States; and

WHEREAS, CHILDREN'S MERCY HOSPITAL, a Corporation duly organized under the laws of the State of Missouri, and having its principal place of business at 2401 Gillham Road, Kansas City, MO 64108, is desirous of acquiring an interest in, to and under said invention, said application and any and all Letters Patent which may be granted for or upon said invention in the United States of America and all countries foreign thereto.

NOW, THEREFORE, to all whom it may concern be it known that for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledge, WE, JOAN H. M. KNOLL and PETER K. ROGAN, as co-inventors, have sold, assigned and transferred, and by these presents do sell, assign and transfer unto said CHILDREN'S MERCY HOSPITAL, the full and exclusive right, title and interest, throughout the world, in, to and under the following:

(a) said invention as fully set forth and described in the specification prepared, and executed by each of such as co-inventors on even date herewith preparatory to obtaining Letters Patent of the United States therefor;

(b) said application;

(c) any and all refilings and continuations of said application;

(d) any and all Letters Patent of the United States of America which may issue from said application, refilings, division and continuations;

(e) any and all reissues of said Letters Patent of the United States of America;

(f) any and all applications for Letters Patent upon said inventing which may hereafter be filed in any and all countries foreign to the United States of America;

(g) any and all refilings, divisions and continuations of said foreign-filed applications;

(h) any and all Letters Patent of countries foreign to the United States of America which may issue from the said foreign-filed applications, refilings, divisions and continuations; and

(i) any and all extension of, and additions to, said Letters Patent of countries foreign to the United States of America.

ALL of the above shall be held and enjoyed by said CHILDREN'S MERCY HOSPITAL for its own use and behoof, and for its successors, legal representatives and assigns, to the full end of the term for which said Letters Patent may be granted, and we do hereby authorize and request the Commissioner of Patents and Trademarks to issue the said Letters Patent in accordance with this Assignment.

Executed this 29 day of August, 2000.

Joan H. M Knoll, Ph.D.
JOAN H. M. KNOLL

Peter K Rogan PhD
PETER K. ROGAN

STATE OF Missouri)
) SS.
COUNTY OF Clay)

" NOTARY SEAL "
James P. Brown, Notary Public
Clay County, State of Missouri
My Commission Expires 6/13/2004

On this 29 day of August, 2000, before me personally appeared JOAN H. M. KNOLL and PETER K. ROGAN, to me known to be the persons described in and who executed the foregoing instrument, and they duly acknowledged to me that they executed the same for the uses and purposes therein set forth.

James P. Brown
Notary Public

My Commission Expires:

06-13-2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Docket No. 30307 CNT1
KNOLL, JOAN et al.	
Serial No. :	Group Art Unit No.
Filed:	
SINGLE COPY GENOMIC HYBRIDIZATION PROBES AND METHOD OF GENERATING THE SAME	Examiner:

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

DECLARATION

WE, JOAN H. M. KNOLL and PETER K ROGAN declare and state as follows:

1. We are the inventors of the subject matter described and claimed in the above-identified patent application. A copy of each of our respective curriculum vitae is attached hereto as Exhibit A.

2. This declaration is being submitted by us pursuant to 37 C.F.R. § 1.132 in order to submit evidence pertaining to what is described in the application and its significance to those of ordinary skill in the art.

3. The claims are directed to a nucleic acid hybridization probe which will hybridize to a nonrepetitive portion of target nucleic acid, said probe comprising a labeled, single copy human nucleic acid sequence of known sequence, said probe having a length of at least about 2000 nucleotides, said probe being free of the repeat sequences identified as SEQ ID Nos. 1-428 and 447-479 and subsequences therof, said subsequences containing at least 17 nucleotides, at

least a portion of the human nucleic acid sequence being derived either from an intron or an intergenic region wherein an intergenic region begins either upstream of the transcription initiation site or downstream of the polyadenylation site, and said probe being complementary to a non-repetitive portion of the target.

4. The significance of such probes is that they are useful for identifying chromosomal variations or abnormalities in individuals as well as identifying where such variations or abnormalities occur in individual's genomes. Such information can then be correlated with specific conditions, cancers, diseases, and syndromes as well as aid in the diagnosis of the same.

5. People of skill in the art are aware that chromosomal abnormalities can appear in any chromosomal band in the human karyotype. Thus, if single copy probes were available for each of the chromosomal bands, hybridization studies using these probes would identify in which band a breakpoint occurred. This knowledge would then help to characterize the ramifications of breakpoint locations and aid in the diagnosis of specific disorders correlated with chromosomal abnormalities at the DNA level.

6. Support for the vast amount of knowledge concerning abnormalities can be found in a wide variety of references. For example, Digamber Borgaonkar in *Chromosomal Variation in Man A Catalog of ChromosomalVariants and Anomalies*, 7th ed. (1996) provides a compilation of inherited chromosome abnormalities including structural variations, deletions, inversions, translocations, trisomies, monosomies, polyploids, and chromosomal breakpoint syndromes. A copy of a representative page, together with a copy of the cover and a copy of the Library of Congress information page is included herein as Exhibit B.

7. The selected page of Exhibit B, (page 10), lists several case studies wherein an abnormality was found in 1p22. One example from this page is from a study by Dhadial, R K and M F Smith. This study identified a terminal 7p deletion and 1;7 translocation associated with craniosynostosis, designated as 46, XX, t(1;7)(p22;p15), del(7)(pter to p15) following the International System for Human Cytogenetic Nomenclature (ISCN (1995)): International System for Human Cytogenetic Nomenclature, Mitel F (ed); S. Karger, Basel, 1995), which is readily understandable by those of skill in the art. Accordingly, whether or not a single copy probe within the 1p22 band hybridized to a proper location could be used to identify and characterize the nature of a breakpoint or abnormality in this band. When the results of the hybridization are correlated with knowledge such as is provided in this reference, it is easy to see the importance and significance of the probes of the present invention.

8. Similarly, the compact disc attached hereto as Exhibit C provides evidence that every chromosomal band in the genome contains at least one site of chromosomal breakage and that many of these breakages are associated with various forms of cancer. The first file in the compact disc is entitled cancer_research_bk1_abnormalities_refsuptoyr2000. This file covers references of such breakpoints up to the year 2000, and therefore contains the knowledge available to those of skill in the art prior to the filing date of the application upon which this continuation application is based. The second file (cancer_research_bk1_abnormalities_refsuptoyrNov03) includes references filed after the filing date of the application upon which this continuation application is based. Each of these files was derived from information published in the Mitelman Database of Chromosome Aberrations in Cancer, which is published in a hard copy version and online at

http://cgap.nci.nih.gov/Chromosomes/Mitelman. The abnormalities present in each band are presented in separate worksheets of these files and the band designation is given on the top line of each worksheet. Further information can be found in the Mitelman Reference Searcher located online at http://cgap.nci.nih.gov/Chromosomes/RefSearchForm. This Reference Database contains the complete set of references for chromosomal aberrations culled from the literature by Mitelman, Johansson, and Mertens. The references are organized into three groups: a)The Individual Case references; b)The Molecular Biology Associations references; and c) The Clinical Associations references. The search engine can find any reference by author, journal, year, or reference number in one, two, or all three of these groups.

9. The single copy probes of the present invention are useful in a variety of contexts including identifying, localizing, diagnosing and characterizing chromosomal abnormalities. Because every chromosomal band includes at least one site of chromosomal breakage, the resulting chromosomal abnormalities are used for selecting single copy probes for hybridization analysis. Furthermore, it is clear that the bands represent a group of related biological structures that are detectable with the single copy probes of the present invention.

10. For example, Reference No. 195 or Case No. 16 of Investigation No. 1 of Oshimura et al., 38 Cancer, 748-761 describes a case of acute erythroleukemia (FAB type M6) having the abnormalities designated as 47, XX, der(1)t(1;13)(p36;q14),t(3;5)(q21;q31),+8,-13,+22. Such a designation refers to a female individual (XX) with 47 chromosomes having a derivative chromosome 1 resulting from a translocation between chromosomes 1 and 13. The translocation in chromosome 1 occurs on chromosomal arm p, region 3, band 6 and the translocation in chromosome 13 occurs on the q chromosomal arm at region 1, band 4. The individual does not have the reciprocal translocation chromosome or derivative chromosome 13

resulting from this translocation. The individual also has a second, unrelated translocation between chromosomes 3 and 5 with the translocation occurring on the q arm, region 2, band 1 for chromosome 3 and on the q arm, region 3, band 1 for chromosome 5. The additional chromosome in the complement (ie. 47 as compared with a normal chromosomal number of 46) arises from having an additional copy of each of chromosomes 8 and 22 and losing a copy of chromosome 13. Single copy probes such as those of the present invention would be very useful in identifying and characterizing similar abnormalities in other individuals and eventually aiding in the diagnosis of such abnormalities and their associated clinical maladies/findings.

11. In some instances, and as can be seen by this example, a plurality of single copy probes would need to be used together in order to fully characterize and/or identify certain abnormalities that involve multiple chromosomes or bands within a single chromosome. Thus, it would be beneficial, and in certain instances, essential, to have the full complement of single copy probes available prior to their use in any individual. If some information regarding the individual is available prior to use of the probes, certain probes may be selected as it is known in which chromosome and band the probes appear in a normal genome. For example, if it is known that the individual has a translocation of a portion of chromosome 1 to a different chromosome, chromosome 1 probes can be used to delineate the locations of specific sequences from chromosome 1 on the translocated chromosome in that individual. Due to their single copy nature, hybridization will only occur at a single homolog location in the genome, unless the individual is aneuploid for that sequence as a result of an abnormality or a polymorphism. Thus, the pattern and location of their hybridization will determine the nature of the translocation. Similarly, if hybridization does not occur, the individual may not contain a copy of the corresponding genetic material which may be the result of an abnormality. At any rate, whether

the probes are used alone or in combination with other probes, the utility of the probes is clear.

12. In all of these examples, ICSN nomenclature is used. The ISCN represents nomenclature standardization for all clinical laboratories worldwide that report cytogenetic abnormalities. Some of the more common abbreviations and their definitions include t (translocation); inc (incomplete karyotype in which not all of the abnormalities can be identified due to the chromosome quality); inv (inversion); mar (marker); i (isochromosomes); ins (insertion); del (deletion); der (derivative); dup (duplication); r (ring); dic (dicentric); idem (denotes the stemline karyotype in subclones); + (extra); and, - (missing). Of course, these and the other abbreviations used are known to the cytogenetic community. Furthermore, such knowledge was available prior to the filing date of the present application.

13. We further declare that all statements made herein of our own knowledge are true and all statements made on information and belief are believed to be true, and further that those statements were made with the knowledge that willful, false statements and the like are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and such willful false statements may jeopardize the validity of any patents issued from the patent application.

Date: Jan 19, 2004

JOAN H.M. KNOLL

Date: Jan 19, 2004

PETER K. ROGAN